

REMARKS

Claims 1-8, 14-20, 53 and 59-60 are pending. Claims 15, 19-20 and 53 were withdrawn from examination. Claims 56-58 have been cancelled in this Response. Claims 1-8, 14, 16 and 18 have been amended. Support for these amendments may be found throughout the specification, for example, original Claim 1; page 6, lines 24-30; page 7, lines 19-31; page 8, lines 20-32; page 4, line 27- page 5, line 2; and page 20, lines 9-33. Claims 59-60 are new. Support for these claims may be found throughout the specification, for example, page 6, lines 2-15.

Claim Rejections under 35 U.S.C. § 101

Claim 1 was rejected under 35 U.S.C. 101 as being directed to non-statutory subject matter. Applicants respectfully submit that amended Claim 1 does not read on a product of nature, as the strain in amended Claim 1 is “genetically engineered.” Applicants respectfully request that this rejection be withdrawn.

Rejection(s) under 35 U.S.C. § 112, 2nd Paragraph

Claims 1-8, 14, 16-18 and 56-58 were rejected under 35 U.S.C. 112, 2nd Paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

Claim 1 was rejected as vague and indefinite due to the description ‘an lgtB⁻nesisserial strain’. Applicants have amended Claim 1 to provide further clarity; support for this amendment may be found throughout the specification, including in original Claim 1 and on page 6, lines 24-30. Applicants respectfully submit that this rejection is now moot and request that it be withdrawn.

Claim 1 was rejected as vague and indefinite because it was not clear to the Examiner whether the L3 LOS is naturally occurring or conjugated to the bleb preparation. Applicants respectfully traverse this rejection and submit that the description ‘a Neisserial strain with an L3 LOS immunotype’ is clear and definite. As described on page 2, lines 16-32, LOS, lipopolysaccharides, are outer membrane bound glycolipids which generate structural and antigenic diversity among different meningococcal strains. Therefore, the recitation that the Neisserial strain of Claim 1

has an L3 immunotype clearly describes the immunotype of the strain. Applicants respectfully request that this rejection be withdrawn.

Claim 1 was also rejected as vague and indefinite due to the term ‘derived.’ Applicants respectfully submit that this rejection is moot in light of the amendments to Claim 1 and request that this rejection be withdrawn.

Claims 4-7 were rejected as vague and indefinite because it was not clear to the Examiner whether it is the ‘downregulation’ of the specified genes which is responsible for the inability to synthesize capsular polysaccharide of Claim 3. Applicants traverse this rejection as to Claim 5-7 as these claims do not depend from Claim 3. Applicants respectfully submit that this rejection is moot in light of the amendments to Claim 4 and request that this rejection be withdrawn.

Claims 56-58 were rejected as vague and confusing because it was unclear to the Examiner how this additional bleb preparation applies to the bleb preparation of Claim 1. Claims 56-58 have been cancelled. Applicants respectfully submit that this rejection is moot and request that it be withdrawn.

Rejection(s) under 35 U.S.C. § 103

Pending Claims 1-8 and 14-18 are patentable over Berthet et al.

Claims 1-8, 14-18 and 56-58 were rejected under 35 U.S.C. 103(a) as being unpatentable over Berthet et al. (WO 01/09350 A2). Applicants respectfully traverse this rejection.

The Supreme Court has stated that the *Graham* factors continue to define the inquiry that controls in determining if the claimed subject matter is obvious under § 103. *KSR Int’l Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (2007). “[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” *Id.* at 1741 (quoting *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006)). Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness for at least the reason that the Examiner has failed to establish a rational underpinning to support the legal conclusion of obviousness based on the *Graham* factors.

Berthet et al. do not disclose or suggest a Neisserial bleb preparation from a Neisserial strain with an L3 LOS immunotype wherein the Neisserial strain has been genetically engineered to permanently down-regulate the expression of functional gene product from the *lgtB* gene. Not only do Berthet et al. fail to exemplify the use of LOS of any immunotype (as recognized by the Examiner, page 6, Office Action mailed March 27, 2008), Berthet et al. also fail to recognize the preferred downregulation of the expression of the functional gene product from the *lgtB* gene (for example, page 31, Berthet et al.). In contrast, it was Applicants who found that *lgtB*⁻ mutants provide a truncation for resolving human red blood cell reaction issues whilst retaining an LOS protective oligosaccharide epitope that can still induce a bactericidal antibody response. (page 6, lines 20-24). The Examiner has failed to provide any evidence suggesting that “mutants of any of the *lgtA-C* genes would have resulted in a detoxified preparation,” as suggested on page 7 of the Office Action. Applicants respectfully submit that it would not have been obvious to one of ordinary skill in the art to use an *lgtB*⁻ strain to produce the blebs.

Furthermore, Gu et al. (US 6,531,131) do not make up for the deficiencies of Berthet et al. Gu et al. relates to a conjugate vaccine for *Neisseria meningitidis* comprising lipooligosaccharide which does not contain a lacto-N-tetraose antigen (abstract, column 1 lines 15-19). In contrast, Applicants’ invention relates to a bleb preparation in which inactivation of the *lgtB* gene results in an intermediate LOS structure, one in which at least a portion of the structure similar to the lacto-N-neotetraose oligosaccharide group is present (page 6, lines 1-23). In fact, Gu et al. actually teach away from Applicants’ bleb preparation. Furthermore, Applicants’ invention yields more than predictable results, it provides for an unexpectedly and fruitful result, one in which epitopes that can elicit a bactericidal immune response are retained, but epitopes that create cross-reaction of the anti-LOS immune response with structures present at the surface of human tissues are not retained. (See, for instance, Examples 3 and 6). Such secondary considerations prove instructive. *Id.* at 1739 (citing *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17 (1966)). The fact that the elements worked together in an unexpected and fruitful manner supports a conclusion that the invention was not obvious to one skilled in the art. *Id.* at 1739-1740 (citing *United States v. Adams*, 383 U.S. 39 (1966)).

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Applicants respectfully submit that pending claims 1-8 and 14-18 are patentable over Berthet et al. and respectfully request that this rejection be withdrawn.

CONCLUSION

Should any outstanding issues remain, the Examiner is encouraged to contact Applicants' undersigned representative.

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